8 Diamond-Blackfan Anemia

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DEFINITION: Diamond-Blackfan anemia (DBA) is congenital pure red cell aplasia.

SYNONYMS: Blackfan-Diamond anemia; Congenital hypoplastic anemia; Chronic congenital aregenerative anemia; Hereditary red cell aplasia; Congenital erythroid hypoplasia; Erythrogenesis imperfecta; Chronic idiopathic erythroblastopenia with aplastic anemia (type Josephs-Diamond-Blackfan); Aase syndrome.

DIFFERENTIAL DIAGNOSIS: Acquired pure red cell aplasia; Transient erythroblastopenia of childhood (TEC); Parvovirus B19 infection; Fanconi anemia; Aplastic anemia; Autoimmune hemolytic anemia.

SYMPTOMS AND SIGNS: Pallor, lassitude, and even congestive heart failure may occur, due to severe anemia. Approximately 30% of patients are diagnosed in the first 3 months of life, 90% in the first year. One third have physical anomalies, such as abnormal thumbs, characteristic facies, or short neck; short stature is common. A substantial risk exists for the development of myelodysplastic syndrome or acute myeloid leukemia, as well as selected solid tumors such as osteosarcomas.

ETIOLOGY/EPIDEMIOLOGY: There are at least three different gene loci for DBA. Approximately 20% have mutations at 19q13 in RPS19, which are inherited in an autosomal dominant manner. The molecular mechanism is not known. Males and females are affected equally, and all racial and ethnic groups have been reported. Diamond-Blackfan anemia is estimated to occur in 5 to 10 per 1million live births.

DIAGNOSIS: Patients with DBA have a macrocytic anemia, with reticulocytopenia and marrow erythroblastopenia. White blood cells and platelets are usually normal. Bone marrow examination distinguishes the red cell underproduction in this condition from erythroid hyperplasia in hemolytic anemias. Erythroid vacuoles and nuclear inclusions suggest parvovirus. Red cell adenosine deaminase is elevated in most patients.

TREATMENT

Standard Therapies: More than half of patients respond to treatment with prednisone. Patients who do not respond to steroids can be transfused with leukocyte-depleted, irradiated, packed red blood cells. Iron overload requires chelation with parenteral desferrioxamine. Remissions occur in approximately 25% of patients, both prednisone-responsive and those solely transfused. Stem cell transplant (with bone marrow or cord blood) is an option for patients with an HLA-matched sibling donor.

Investigational Therapies: Researchers are investigating stem cell transplant for DBA from alternative donors.

REFERENCES

Alter BP, Young NS. The bone marrow failure syndromes. In: Nathan DG, Orkin SH, eds. *Nathan and Oski's hematology of infancy and childhood,* 5th ed. Philadelphia: WB Saunders, 1998:237–335.

Draptchinskaia N, Gustavsson P, Andersson B, et al. The gene encoding ribosomal protein S19 is mutated in Diamond-Blackfan anaemia. *Nat Genet* 1999;21:169–175.

McKusick VA, ed. Online Mendelian Inheritance in Man (OMIM). Baltimore, MD: The Johns Hopkins University. Entry no. 205900; last update 7/27/2000.

Willig TN, Niemeyer CM, Leblanc T, et al. Identification of new prognosis factors from the clinical and epidemiologic analysis of a registry of 229 Diamond-Blackfan anemia patients. *Pediatr Res* 1999;46:553–561.

Willig TN, Perignon JL, Gustavsson P, et al. High adenosine deaminase level among healthy probands of Diamond Blackfan anemia (DBA) cosegregates with the DBA gene region on chromosome 19q13. *Blood* 1998;92:4422–4427.

RESOURCES

133, 134, 356